1652

TRANSMITTAL LETTER (General - Patent Pending)	Docket No. 46906-DIV2 (71699)

In Re Application Of: S. Chatterjee

Serial No.	Filing Date	Examiner	Group Art Unit
09/282,879	March 31, 1999	M. Rao	1652

Title: **RECOMBINANT N-SMASES AND NUCLEIC ACIDS ENCODING SAME**

TO THE COMMISSIONER FOR PATENTS:

Transmitted herewith is:

Supplement Declaration Pursuant To 37 CFR 1.132;
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in the above identified application.

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Dated: 6 June 03

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Docket No. 46906-DIV2 (71699)

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

APPLICANT: S. Chatterjee

SERIAL NO.: 09/282,879 EXAMINER: M. Rao

FILED: March 31, 1999 GROUP: 1652

FOR: RECOMBINANT N-SMASEs AND NUCLEIC ACIDS ENCODING SAME

THE HONORABLE COMMISSIONER OF PATENTS AND TRADEMARKS
WASHINGTON, DC 20231

SIR:

SUPPLEMENTAL DECLARATION PURSUANT TO 37 CFR 1.132

The undersigned declares as follows:

1. I am the inventor of the above-identified application (hereafter the "subject application"). Additionally, I am a Professor of Pediatrics in the Department of Pediatrics at the Johns Hopkins University Medical School in Baltimore, MD.

2. As I understand it, the subject application discloses and claims, among other things, a method of identifying a compound useful in the diagnosis or treatment of a human neutral sphingomyelinase (N-Smase) related disorder. A particular method includes contacting an agent with a recombinant N-Smase and analyzing enzyme activity in the presence and absence of the agent.

3. I have reviewed the Patent Office Action ("Office Action") dated November 27, 2002 issued in connection with the subject application. As I understand the Office Action, the patent Examiner rejected claims 13-17 and 31 as being obvious over Chatterjee et al. (*J. Biol. Chem.* (1989) 264: 12554); Ogita et al. (WO 95/18119); and Ausbel et al. (*Current Protocols in Molecular Biology*, J. Wiley & Sons (1987) pp. 10.0.3

-10.06). Hereinafter, the cited references are referred to as "Chatterjee", "Ogita" and "Ausbel", respectively.

4. I am familiar with the contents of Chatterjee and Ausbel and I have read an English language translation of Ogita. As I understand it, Chatterjee reports isolation of naturally-occurring N-Smase from human urine, Ogita (as translated) reports isolation of a bacterial sphingomyelinase inhibitor from grass, and Ausbel discloses standard cloning methods.

5. I must respectfully disagree with the patent Examiner's position that the method I now claim is obvious over Chatterjee, Ogita and Ausbel. More specifically, I must disagree with the suggestion by the Examiner that it would be obvious to make the recombinant N-Smase featured in the claimed method.

6. For example, I have encountered substantial problems using the naturally-occurring N-Smase of Chatterjee et al. with the claimed method.

7. In particular, I found that even when the natural N-Smase enzyme is highly purified, it includes tightly associated proteases and phosphatases. Unfortunately, these enzymes degrade the enzyme. That activity renders the natural enzyme unsuitable for use with the claimed method. In contrast, the recombinant N-Smase of claim 1 is not associated with any detectable protease or phosphatase activity.

8. I also found that storage of the natural N-Smase enzyme, particularly long term, lowers its specific activity for substrate. This makes that natural enzyme unsuitable for use with the claimed method. Unlike that enzyme, the recombinant N-Smase of claim 1 is more stable. Use of the recombinant enzyme in the claimed method results in better sensitivity and reproducibility, for example.

9. In addition, storage of the natural N-Smase enzyme produces multiple proteolytically digested products. These products are not desirable for use with the claimed method. For example, one or more of the products can contribute to false or misleading identification of compounds according to the claimed method. In marked contrast, I have found that storage of the recombinant N-Smase of claim 1 does not result in detectable production of the digestion products.

10. As I understand the Chatterjee, Ogita and Ausbel references as cited by the Examiner, none of them disclose or suggest the foregoing problems of using the natural N-Smase enzyme with the claimed method.

11. I hereby further declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true, and further that these statements are made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

Date: May 28, 03

Subroto Chatterjee

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